Review of Draft GuLF Worker Study Protocol
September 14, 2010

This is a review of the September 7, 2010 Draft of the GuLF Worker Study Protocol provided to the IOM. My review focuses primarily, but not exclusively, on aspects of exposure assessment for the prospective epidemiological investigation.

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Overview Comment:
Overall, the investigators have developed a well-designed and comprehensive protocol for investigating the short- and long-term health of oil spill clean-up workers and volunteers following the Deepwater Horizon oil spill. Exposure assessment in this study presents numerous challenges due to the multiple chemicals of interest, the limited personal measurement data, the varied work tasks involved, and the socially and geographically diverse population. The proposed expert development of a Job Exposure Matrix, informed by limited exposure measurement data, is the best available approach for exposure assessment. However, both the worker and control populations are likely to have wide ranges in occupational and non-occupational exposures to many of the chemicals of interest, unrelated to the oil spill. Thus, adequate data will need to be collected and considered in the analysis to minimize, to the extent feasible, confounding and exposure misclassification.

General Comments:
1) There is limited information or discussion in the protocol regarding development of the exposure metrics. At this stage of protocol formation the lack of detail in understandable as metric development will be complex and require a great deal of effort and review. An expert panel will develop a Job Exposure Matrix (JEM) based on the varied work tasks of cleanup workers and volunteers. The protocol describes the use of a dichotomous (yes/no) exposure metric and an ordinal (1-5) JEM-based ranking of exposure intensity. However, different dichotomous and ordinal ranking metrics may need to be developed for different chemicals and exposure pathways that could – potentially – result in different health effects. For example, a single metric will probably not capture the important differences in particle inhalation exposures among oil burn workers versus dermal PAH exposure of absorbent boom operators. The exposure metrics will not only need to consider differential exposures based on job task, but will also need to consider the duration of exposures (hours per day, total days of work).

2) If sufficient worker personal monitoring data are available across different job tasks they will be informative in developing JEMs and may provide useful information regarding the general range and differences in exposure magnitude. If known, it would be useful to include in the protocol some general information regarding the types and extent of measurement data that might be available to inform exposure metric development.

3) One of the challenges of this research is that most workers and controls will have exposures, unrelated to the oil spill, to many of the chemicals of interest. Virtually all persons are exposed to benzene in ambient air (usually at very low levels) and to PAHs from inhalation, dietary ingestion, and house dust. There are also a number of consumer products that contain 2-butoxyethanol or propylene glycol, two possible dispersant ingredients of interest. Some workers and controls could have significant exposures to some of these chemicals due to their occupations. In most cases, these types of "background" exposures are likely to have similar distributions among the worker and control populations. However, the study will need to carefully consider and collect information to understand when this might not be the case. Two examples:

a) Commercial boat operators that participated in cleanup activities could – potentially – receive higher long-term exposures to fuel oil and engine exhaust, with many of the same chemical constituents as found in the spilled oil, as compared to a control group that did not include active boat operators.

b) Workers may come from Gulf coast locations impacted by point sources of petrochemical pollution not experienced by the control groups living inland or in other states.

It seems likely that these potentially confounding exposure situations would be more likely to affect long-term health outcome assessments. Potential confounding impacts can be addressed through adequate questionnaire data collection (occupational and other relevant activities/exposures) and possibly augmented with GIS mapping.

Specific Comments:
4) Section 3.1.1: The stated goal is to capture a representative sample of clean-up workers and controls. However, in subsequent sections, there is little information regarding the details of enrolling a representative sample – particularly for controls.

5) Section 3.1.2: The number of controls for the Biomedical Surveillance Sub-cohort is not specified. Given the relatively low ratio of controls to workers in the overall cohort, will there be a sufficient number of controls in this sub-cohort to support adequate statistical analyses?

6) Section 3.1.3: It is not clear that the tap water and dust samples are being collected and stored in a way that will allow valid measurement of many of the chemicals of possible interest in this study. See later comments.

7) Section 3.2: Will there be any attempt, perhaps using a small sub-sample of workers, to verify self-reports that they actually did clean-up work? Are there records available for this type of assessment – pay records, records of waste collected, etc?

8) Section 3.2: It is not clear how a representative sample will be enrolled into to the active and passive cohorts given the fairly subjective criteria of being suspected of "high" and "lower" exposures. Are there sufficient extant data to develop a sampling frame that would allow representative over-sampling of the "high" exposures into the active cohort?

9) Section 3.9: The second paragraph describes how the biospecimens will be shipped and processed. The environmental samples, however, are not mentioned here.

10) Section 3.9.3: It is good that the questionnaire will include modules to collect information on occupational exposure to the target chemicals unrelated to oil spill work. However, there are non-occupational exposures that might be considered as well. For example, dietary intake and ETS exposure can be important for PAHs; use and storage location of gasoline can be important for benzene.

11) Section 3.9.5: If feasible, it is recommended that the full void of urine be collected, the volume of the sample be measured or estimated, and that the time of day for the previous void be collected.

12) Section 3.9.5: A urine dipstick will be used to measure several urine parameters. Will these metrics be used to direct more quantitative lab analyses when abnormal readings are obtained, or will they be used as primary metrics in outcome analyses? Given the mixed results for specificity and sensitivity reported in the literature for dipstick measures, if they are used as primary outcome variables, it is recommended that a relevant subset be also analyzed using quantitative laboratory procedures to assess performance.

13) Section 3.9.6: It is not clear why tap water and household dust are being collected. This is important, because the subsequent handling and storage procedures may not be adequate for some analytes that might be of interest. For example, if there is interest in measuring VOCs, metals, or other organics in water, then the standard methods call for different collection procedures, preservatives, shipping and storage temperatures, and analysis within specific holding times. If the dust samples will are intended for future analyses of organic compounds (PAHs for example – or the pesticides and phthalate mentioned in this section) then shipment and long-term storage at ambient temperatures is not acceptable. Also, if phthalates are truly of interest, then it will be very important to verify that the collection and storage materials are phthalate free and remain phthalate free over long storage times.

14) Section 3.11.1: See above comments regarding shipping and storage conditions for tap water and house dust samples.

15) Section 3.11.3: Are there any plans to measure V and Ni in urine and/or blood samples? While the time between oil exposure and sample collection will likely make these not useful as oil-spill exposure biomarkers, they might be relevant if there are ongoing clean-up activities or other occupational exposures to oil or oil products. These elements seem somewhat more relevant for oil exposures than the As, Cd, Cr, Mn, and Pb mentioned in the protocol.

16) Section 7.4: It is recommended that tap water and dust samples also be collected from the 200-person external group. It will be very important to assess QA/QC and long term storage viability in these media.

17) Section 7.5.2: Consider including the Biomedical Surveillence Sub-Cohort to the power and detectable difference tables. It is not clear how many controls will be included in the Sub-cohort and what level of analyses can be supported. This may be important for subsequent decisions on the measurements in the sub-cohort.

18) Section 9.1.2: Given the large number of independent in-field HVAs planned for the study (n=140) and field supervisors (n=10), there is a very real potential for disparate data collection even if very strong SOPs are developed. (Will SOPs be developed prior to training?) Given the complexity of the protocol, and the importance of comparability across 140 HVAs, will two days of HVA training and practice be adequate? Consider adding at least one more training/evaluation day. Ensure that the in-training evaluations and subsequent in-field evaluations are adequate for providing as much comparability among HVAs as possible. Consider having one very experienced overall field supervisor that will be able to do across-group evaluations at the beginning of the study and at other time points later in the study. (Are any objective measures being developed for evaluation of comparability?)